An Elderly Patient With a Positive Preoperative Stress Test Presents for a Semiurgent Vascular Surgery

Kyung W. Park, M.D. Boston, Massachusetts

OBJECTIVES

1. To become familiarized with the American Heart Association's guidelines on preoperative cardiac evaluation.
2. To discuss the role of preoperative cardiac evaluation in triage of presurgical patients and know the risks and benefits of alternative management strategies.
3. To discuss and formulate a strategy for perioperative beta-blockade.

STEM CASE - KEY QUESTIONS

A 72 year old white male with a history of coronary artery disease, diabetes mellitus, hypertension, and hypercholesterolemia was admitted with a non-healing ulcer and cellulitis of his left heel. He had had a coronary artery bypass surgery 7 years ago and occasionally gets exertional angina. His diabetes was diagnosed 20 years ago and has been treated with insulin for the last 10 years. He has diabetic peripheral neuropathy in the lower extremities and this, along with his peripheral vascular disease, has been limiting his exercise capacity. His medications on admission included NPH insulin 36 units q AM and 24 units q PM with a sliding scale of regular insulin, amlodipine 10 mg q d, baby aspirin 1 tablet a day, and atorvastatin 10 mg q day. An angiogram of the left leg demonstrated patent common femoral and superficial femoral arteries, but diffuse narrowing of the popliteal and anterior tibial arteries and occlusion of the posterior tibial artery. The vascular surgeon wants to perform a femoral-anterior tibial bypass with debridement of the left heel ulcer.

1. What is the patient's cardiovascular risk profile for the proposed surgery? Does the patient need cardiology consultation and further cardiac workup prior to undergoing the vascular surgery? If so, which tests may be indicated and what information do they offer us?

His vascular surgeon decides to send the patient to the cardiologist for consultation, who orders a dipyridamole-thallium study. During the test, the patient reaches 56 % of his maximum predicted heart rate. The study shows a mild reversible perfusion defect in the inferolateral wall, suggestive of ischemia, as well as a fixed inferior defect. Overall left ventricular ejection fraction was estimated to be 45 %.

2. How is a dipyridamole-thallium study performed? Was this an appropriate stress test for this patient? What is the significance of a "mild reversible perfusion defect"? Of a "fixed defect"?

3. In view of the positive result on the dipyridamole-thallium study, what should be an appropriate triage to manage this patient further? If the patient were referred to cardiac catheterization and then coronary revascularization, what would be the risk of the combined procedures? If he survives coronary revascularization either by surgery or percutaneous intervention, how long does he need to wait before he can safely undergo a vascular surgery?

In fact, the cardiologist recommends that the patient can undergo vascular surgery safely without prior coronary revascularization and "clears" the patient for leg revascularization. He also

recommends that the patient should be started on metoprolol 25 mg q d, with the dose gradually increased as tolerated in order to bring the patient's heart rate down to 70. However, the surgeon has already scheduled the patient for surgery in 2 days.

4. What is the basis, if any, of the cardiologist's recommendation to proceed with surgery after a positive result on the dipyridamole-persantine test? If one may assume that the patient would have been recommended for surgery with a negative stress test as well, what was the point of ordering the stress test? If the patient's left ventricular ejection fraction had been 20 %, should the cardiologist's recommendation have been different?

5. What is the current literature evidence documenting the benefit of perioperative beta-blockade? What is the basis, if any, of recommending to bring down the heart rate to a target rate of 70 or less? How long prior to surgery should the patient be started on a beta-blocker, in order to benefit from it?

6. Are there any contraindications to perioperative beta-blockade? Are there any differences among different beta-adrenergic blockers? In patients who are not able to take a beta-blocker, is there an alternative medical regimen one may offer?

You agree to provide anesthesia for this patient and visit the patient to discuss anesthetic options and risks. The patient says, "Doc, I want you to be honest with me. Am I going to die during this surgery? But I don't want to lose my leg, either."

7. How would you approach the patient's comments and question? What is a realistic estimate of the patient's morbidity and mortality?

8. After the patient survives the surgery with your expert care, what should be an appropriate follow-up care for this patient? Should the beta-blocker be continued indefinitely for this patient? If not, why not and how long is an appropriate interval for perioperative beta-blockade?

PROBLEM BASED LEARNING DISCUSSION

1. What is the patient's cardiovascular risk profile for the proposed surgery? Does the patient need cardiology consultation and further cardiac workup prior to undergoing the vascular surgery? If so, which tests may be indicated and what information do they offer us?

The American College of Cardiology (ACC) and the American Heart Association (AHA) published guidelines on preoperative cardiac evaluations in 1996, with input from the disciplines of anesthesiology, cardiology, electrophysiology, vascular surgery, vascular medicine, and noninvasive cardiac testing (1). The guidelines were updated in 2002 (2). The guidelines consider the urgency of the operation, the recency of cardiac evaluation and intervention, the patient's clinical predictors of cardiac risk, functional status, and the risk of the surgery proposed, in helping to decide whether any further cardiac evaluation is indicated before surgery. For non-emergent operations, if the patient has not had a coronary revascularization within the last 5 years and a favorable cardiac evaluation within the last 2 years without any intervening change in cardiac symptoms or signs, then a further cardiac workup is indicated (a) if the patient has a major clinical predictor, (b) if the patient has an intermediate clinical predictor and poor

functional status and is about to undergo an intermediate-risk surgery, or (c) if the patient has an intermediate clinical predictor or poor functional status and is about to undergo a high-risk surgery. Definitions and examples of these are in references (1) and (2).

In the present case, the patient is about to undergo a peripheral vascular bypass procedure, considered to be a high-risk surgery, generally associated with > 5 % incidence of perioperative cardiac events. In addition, he has insulin-dependent diabetes mellitus, which is an intermediate clinical predictor. His functional status cannot be accurately assessed because of his inactivity. If one follows the ACC/AHA guidelines, then this patient should have a preoperative cardiac workup because of the high-risk surgery proposed and the presence of an intermediate clinical predictor.

2. How is a dipyridamole-thallium study performed? Was this an appropriate stress test for this patient? What is the significance of a "mild reversible perfusion defect"? Of a "fixed defect"?

A dipyridamole-thallium study is a type of a pharmacological stress test (3). Dipyridamole is a coronary arteriolar dilator, which can cause malredistribution of coronary blood flow away from collateral-dependent regions, which then become ischemic. Thallium-201 is a radioactive isotope, that distributes to the perfused parts of the myocardium, emits gamma rays, and allows nuclear imaging of the myocardium to be obtained both within 5-6 minutes of infusion of dipyridamole and then the recovery phase 3-4 hours later. Areas of the myocardium not imaged are said to have perfusion defects. Perfusion defects that persist on both images are "fixed defects" and indicate preexisting myocardial infarction. Perfusion defects that disappear after recovery from dipyridamole are "reversible defects" and indicate transient myocardial ischemia and thus areas at risk. A "mild" reversible perfusion defect indicates that the area at risk is small and not expected to impact greatly on overall myocardial function, even in the event of an ischemic event.

3. In view of the positive result on the dipyridamole-thallium study, what should be an appropriate triage to manage this patient further? If the patient were referred to cardiac catheterization and then coronary revascularization, what would be the risk of the combined procedures? If he survives coronary revascularization either by surgery or percutaneous intervention, how long does he need to wait before he can safely undergo a vascular surgery?

Clearly, this patient has an uncorrected coronary artery disease affecting the inferolateral wall. This condition may be treated either medically or interventionally (either angioplasty or coronary artery bypass surgery (CAB)). Studies conducted in the 1970's and 1980's demonstrated that surgical therapy may be preferable to medical therapy in patients with stenosis of the left main coronary artery or in patients with three-vessel coronary artery disease with left ventricular dysfunction, but there appears to be no clear benefit of surgery for other patients with coronary artery disease (CAD) (4). With the introduction of an aggressive cholesterol-lowering regimen, medical therapy may now be associated with a much lower rate of cardiac events than in the 1980's. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive druG Evaluation) trial is currently examining the relative benefits of medical vs. surgical therapy for CAD (5). According to the Society of Thoracic Surgery database, the mortality of elective re-do CAB was 5.4 %, which may go higher for those in their 70's. Since the risk of re-do CAB

may be higher than the risk of the peripheral bypass surgery, the decision on whether to refer this patient to surgery is not an automatic one.

Studies comparing percutaneous transluminal coronary angioplasty (PTCA) and medical therapy have shown that angioplasty improves exercise performance and reduces coronary symptoms to a greater extent than standard medical therapy, but may be associated with a slightly increased risk of major cardiac events such as MI and death (6-8). In the second Randomized Intervention Treatment of Angina (RITA-2) trial, the rate of death or MI was 6.3 % in patients treated with PTCA and 3.3 % for medically treated patients over a median follow-up period of 2.7 years (8). So, PTCA may not confer any survival benefit to conservative medical therapy. In addition, patients who undergo PTCA with a stent and then undergo a noncardiac surgery within 40 days may face an unusually high mortality (20 % in the report by Kaluza et al. (9)), either from restenosis of the stent or from excessive bleeding. If the noncardiac surgery cannot wait for more than 40 days, perhaps PTCA should not be considered as a preoperative therapy for coronary revascularization.

4. What is the basis, if any, of the cardiologist's recommendation to proceed with surgery after a positive result on the dipyridamole-persantine test? If one may assume that the patient would have been recommended for surgery with a negative stress test as well, what was the point of ordering the stress test? If the patient's left ventricular ejection fraction had been 20 %, should the cardiologist's recommendation have been different?

In a European study, Poldermans et al. (10) investigated 112 patients undergoing abdominal aortic or infrainguinal vascular bypass procedures, who had new reversible wall motion abnormalities on dobutamine stress echocardiography. Patients who had extensive wall motion abnormalities or echocardiographic suggestion of a severe 3-vessel CAD or left main coronary artery disease were excluded. They were randomized to receive either bisoprolol, starting at least 1 week prior to surgery, or a placebo. The bisoprolol group was given additional doses of metoprolol as needed to maintain the heart rate at 80 or less in the perioperative period. Bisoprolol was found to reduce 30-day mortality from 17 to 3.4 % and nonfatal MI from 17 to 0 %. This study demonstrates that even patients who have positive preoperative stress tests may undergo a high-risk noncardiac surgery such as vascular surgery with relatively low mortality and morbidity, when appropriate beta-blockade is utilized. This study may have been a basis for the cardiologist's recommendation to proceed with surgery in this patient.

In retrospect, the dipyridamole-thallium study did not provide any value in helping to triage this patient. However, depending on the practice style of the anesthesiologist involved, the result of the study may have some effect on the level of intraoperative monitoring, the use of perioperative beta-blockade, and perhaps selection of anesthetic medications. It should also be noted that if the patient's ejection fraction had been found to be lower, e.g., 20 %, the cardiologist's recommendation might (or might not) have been different. Although patients with low ejection fractions were officially excluded from Poldermans et al.'s study, the authors did follow and reported on such patients. Of 8 such patients, 4 underwent CAB and 2 of these died. The other 4 underwent vascular surgery without prior coronary revascularization but with perioperative beta-blockade. None of these 4 died, but one had a perioperative MI. So the suggestive evidence appears to be that even in patients with low ejection fractions or extensive wall motion abnormalities, the safer course may be to proceed with vascular surgery with

appropriate beta-blockade, rather than to go to coronary revascularization before vascular surgery. More data is needed on this subject, however, before any definitive recommendations may be made.

5. What is the current literature evidence documenting the benefit of perioperative beta-blockade? What is the basis, if any, of recommending to bring down the heart rate to a target rate of 70 or less? How long prior to surgery should the patient be started on a beta-blocker, in order to benefit from it?

Besides the study by Poldermans et al. (10) cited above, there are many other studies documenting the benefit of perioperative beta-blockade (11-16). The benefit is not exclusive to bisoprolol or any one specific beta-adrenergic blocker, but appears to be a class effect. Although no clear reason has been given for selection of the heart rate of 70 as the target rate, most studies appear to use that number as the target. The study of Poldermans et al. (10) used a target of 80 or less, but in actuality the study group had a median heart rate of about 70, whereas the control group had a median heart rate of about 80. In patients in whom the ischemic threshold heart rate (the heart rate above which ischemia is inducible on a preoperative stress test) is known, Raby et al. advocates maintaining the heart rate 20 % below such a threshold rate (14), but no rationale for choosing 20 % has been given.

Whereas Poldermans et al. started bisoprolol at least 7 days prior to surgery, other authors gave the first dose of a beta-blocker as late as right before anesthetic induction (e.g., 11,12) and still claim to have noted a beneficial effect. The earlier you start the beta-blocker of your choice, the more time you will have to titrate the medication to an appropriate level to achieve a desired heart rate and deal with any side effects of the medication.

6. Are there any contraindications to perioperative beta-blockade? Are there any differences among different beta-adrenergic blockers? In patients who are not able to take a beta-blocker, is there an alternative medical regimen one may offer?

In general, perioperative use of a beta-blocker is considered contraindicated in patients with decompensated congestive heart failure (CHF), a bronchospastic disease (especially for a nonselective beta blocker), bradyarrhythmia or significant heart block not corrected by a pacemaker, or an allergy to the medication (17). Yet anecdotal evidence exists that beta-blockers, especially beta-1 selective blockers, are well tolerated even in patients with bronchospastic diseases and in patients with a history of CHF. Previously cited studies on perioperative beta-blockade also document how well the beta-blockers are tolerated.

A possible alternative to beta-blockers, in case of a drug allergy, may be an alpha-2 agonist such as clonidine, dexmedetomidine, or mivazerol. Alpha-2 agonists may benefit the patient by a similar mechanism of controlling the heart rate and myocardial oxygen demand and may be similarly contraindicated in patients with bradyarrhythmias or heart blocks. A meta-analysis of the literature on perioperative use of clonidine showed that whereas myocardial ischemia might be reduced, the incidence of MI or death did not decrease (18). A more encouraging result has been obtained with mivazerol in vascular surgical patients (19), but this medication is currently unavailable in the U.S.

7. How would you approach the patient's comments and question? What is a realistic estimate of the patient's morbidity and mortality?

As always, one should be truthful and realistic in dealing with this high-risk patient. We may base our comments on studies such as Poldermans et al. (10) and advise the patient that with appropriate care, the expected mortality is around 3.4 %. If any institution-specific data are available, then such data may be quoted and would be more convincing.

An often-asked question in a case like this would be whether the choice of anesthesia has a significant effect of perioperative morbidity and mortality. Although this is a controversial topic, most authors would agree that the type of anesthesia has little effect on mortality or morbidity (20, 21)

8. After the patient survives the surgery with your expert care, what should be an appropriate follow-up care for this patient? Should the beta-blocker be continued indefinitely for this patient? If not, why not and how long is an appropriate interval for perioperative beta-blockade?

What constitutes an appropriate follow-up of patients who have been started anew on a beta-blocker in the perioperative period has not been determined. In my opinion, if the medication is well tolerated without significant side effects, then the patient for whom beta-blockade has been considered to be indicated in the perioperative period should also be considered to have an indication for the medication in the ensuing period, which may be indefinite. Literature data on this point are currently lacking and are sorely needed.

REFERENCES

1. ACC/AHA Task Force Report: Special Report: Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Circulation 1996; 93:1278-1317.
2. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, Fleisher LA, Froehlich JB, Gusberg RJ, Leppo JA, Ryan T, Schlant RC, Winters WL, Jr.
ACC/AHA Guideline Update for Perioperative Cardiovascular Evaluation for Noncardiac Surgery – Executive Summary: a report of the ACC/AHA task force on practice guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) J Am Coll Cardiol 2002; 39:542-553
3. Liao T, Park KW. Noninvasive tests of myocardial perfusion: stress tests and their values. Int Anesthesiol Clin 2001; 39:1-10
4. Bonow RO, Epstein SE. Indications for coronary artery bypass surgery in patients with chronic angina pectoris: implications of the multicenter randomized trials. Circulation 1985; 72:V23-30
5. Maron DJ. Percutaneous coronary intervention versus medical therapy for coronary heart disease. Curr Atheroscler Rep 2000; 2:290-6
6. Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenosis. J Am Coll Cardiol 1995; 26:1600-5

7. Parisi AF, Folland ED, Hartigan P, Veterans Affairs ACME Investigators. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. N Engl J Med 1992; 326:10-6
8. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. Lancet 1997; 350:461-8
9. Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol 2000; 35:1288-94
10. Poldermans D, Boersma E, Bax JJ, Thomson IR, van de Ven LL, Blankensteijn JD, Baars HF, Yo TI, Trocino G, Vigna C, Roelandt JR, van Urk H. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. N Engl J Med 1999; 341:1789-94
11. Mangano DT, Layug EI, Wallace A, Tateo I. Multicenter Study of Perioperative Ischemia Research Group. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. N Engl J Med 1996; 335:1713-20
12. Wallace A, Layug B, Tateo I, Li J, Hollenberg M, Browner W, Miller D, Mangano DT. Prophylactic atenolol reduces postoperative myocardial ischemia. Anesthesiology 1998; 88:7-17
13. Poldermans D, Boersma E, Bax JJ, Thomson IR, Paelinck B, van de Ven LL, Scheffer MG, Trocino G, Vigna C, Baars HF, van Urk H, Roelandt JR. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Bisoprolol reduces cardiac death and myocardial infarction in high-risk patients as long as 2 years after successful major vascular surgery. Eur Heart J 2001; 22:1353-8
14. Raby KE, Brull SJ, Timimi F, Akhtar S, Rosenbaum S, Naimi C, Whittemore AD. The effect of heart rate control on myocardial ischemia among high-risk patients after vascular surgery. Anesth Analg 1999; 88:477-82
15. Stone JG, Foex P, Sear JW, Johnson LL, Khambatta HJ, Triner L. Myocardial ischemia in untreated hypertensive patients: effect of a single small oral dose of a beta-adrenergic blocking agent. Anesthesiology 1988; 68:495-500
16. Urban MK, Markowitz SM, Gordon MA, Urquhart BL, Kligfield P. Postoperative prophylactic administration of b-adrenergic blockers in patients at risk for myocardial ischemia. Anesth Analg 2000; 90:1257-61
17. Warltier DC. ß-adrenergic-blocking drugs: incredibly useful, incredibly underutilized. Anesthesiology 1998; 88:2-5
18. Nishina K, Mikawa K, Uesugi T, Obara H, Maekawa M, Kamae I, Nishi N. Efficacy of clonidine for prevention of perioperative myocardial ischemia: a critical approach and meta-analysis of the literature. Anesthesiology 2002; 96:323-9
19. Oliver MF, Goldman L, Julian DG, Holme I. Effect of mivazerol on perioperative cardiac complications during noncardiac surgery in patients with coronary heart disease: the European Mivazerol Trial (EMIT). Anesthesiology 1999; 91:951-61
20. Breen P, Park KW. General Anesthesia v. Regional Anesthesia. Int Anesthesiol Clin 2002; 40:61-72
21. Bode RH, Lewis KP, Zarich SW, Pierce ET, Roberts M, Kowalchuk GJ, Satwicz PR, Gibbons GW, Hunter JA, Espanola CC, Nesto RW. Cardiac outcome after peripheral vascular surgery. Anesthesiology 1996; 84:3-13
You may contact the author for any additional references.

LEARNING SUMMARY

1. To become familiarized with the American Heart Association's guidelines on preoperative cardiac evaluation.
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